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Trial and error

Italian officials should not go ahead with expensive clinical tests of an unproven stem-cell therapy that has no good scientific basis.

The Italian government is planning to oversee a clinical trial of a controversial stem-cell therapy. There are many reasons for the trial to be stopped — and no good reason for it to be carried out.

Last week, *Nature* revealed that the method used by Italian researcher Davide Vannoni, founder of the Stamina Foundation in Brescia, to treat scores of very sick patients is based on flawed data. The revelation struck a major nerve, and hit the front pages of the main newspapers in Italy, as well as featuring on television and radio talk shows. A highly emotional debate about whether Stamina therapy works, or could ever work, has been running long and hot for months. Vannoni denies any wrongdoing.

The reverberations of *Nature*'s exposé are still being felt. Negative coverage in Italian newspapers has featured patients who received the Stamina therapy on compassionate grounds. At the same time, pro-Vannoni demonstrations have been organized by families of patients who see him as their last hope. Now scientists — as well as some politicians — are questioning whether the ministry of health should continue with the €3-million (US$3.9-million) clinical trial of the technique that it agreed to support in May. It should not.

In large part, the government-sponsored trial was intended as a pragmatic attempt to put the matter to rest: if the method failed, the Stamina Foundation would have no grounds for continuing to push it. To go on with the trial now, given the therapy's uncertain scientific basis, would be absurd.

Vannoni has provided no details of his clinical protocols, referring instead to the scanty methods in his 2010 US patent application. That describes a method for promoting the differentiation of bone-marrow-derived stem cells into other cell types for therapeutic use, and includes two micrographs purporting to document the successful creation of nerve cells. Both, *Nature* revealed, were lifted from papers published by Ukrainian and Russian scientists (see *Nature* http://doi.org/m57; 2013).

The very unlikeliness of the Stamina story should have made the Italian government extremely wary. Vannoni claims to be executing cures that he prefers to conduct without oversight by independent parties. He has provided no detailed protocol to the authorities even though his treatment is invasive — it involves drawing marrow from the bones of patients, manipulating the cells *in vitro* (ostensibly to condition them into becoming healing stem cells) and injecting them back into the patients' veins or spinal cord. He insists that his therapy can only be prepared by his own people, without using good manufacturing practice (GMP). His operation has moved from city to city as public prosecutors try to pin him down.

Vannoni is not a qualified doctor, but a teacher of general psychology at the University of Udine. His response to critics tends to be indirect — stating that they have vested interests, or that they want to stop him from helping those who would otherwise die. He dismisses the only real test so far of his therapy, by doctors in Trieste, saying that the outcome was negative because they used GMP.

Movement of any therapy into a clinical trial requires much more transparency. It also needs a solid theoretical basis for why it should work, backed by scientific evidence, either published or presented confidentially to the appropriate authority, in this case the Italian Medicines Agency. Vannoni has not provided this. Indeed, there is no convincing evidence in the literature to suggest that the mesenchymal stem cells found in bone marrow, which can generate bone, fat and cartilage, can be coaxed into producing nerve or any other cell type that Vannoni has claimed is the basis of his cure.

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Although there are no scientific reasons to justify the trial, Italian officials have mooted a legal one. Various courts in Italy have ruled that individual patients demanding compassionate therapy from Stamina have the right to it, whereas others have ruled that they do not. But that is not sufficient: human experimentation to settle legal differences of opinion is not ethically justified.

Stem cells have huge potential to treat currently incurable diseases and scientists are working systematically to this end. A trial that could bring stem cells into disrepute will hinder their efforts. As Irving Weissman, director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine in California, says: "If the Italian government uses money that could have gone to research that will deliver real stem-cell therapies in the future, a whole cohort of people will die because these therapies had not yet been invented." ■

In the dark

Germany's main funding agency must specify how it will deal with false charges of misconduct.

When it comes to the thorny issue of scientific misconduct and how to police it, Germany is a role model for many. Its main research-funding agency, the DFG, published exemplary guidelines in 1998 to steer good scientific practice in universities.

The guidelines comprise 16 recommendations, and are effectively mandatory because universities that do not sign up to them are not eligible to receive DFG grants. Among the recommendations are mechanisms to drum the importance of honesty into trainee scientists, and a requirement for each university to appoint an independent mediator to whom young scientists can turn in confidence in cases where they suspect misconduct. The DFG also created a central ombudsman